REMARKS

Claims 1-11 are pending and stand for further action on the merits.

The claims have been amended to recite a subset of compounds as originally claimed, to be used in the treatment of a mammal having pollakiuria and/or urinary incontinence.

Claim 1 has been amended to recite the treatment of pollakiuria and/or urinary incontinence. Support for the maladies of pollakiuria and/or urinary incontinence can be found in claim 5.

Also, claim 1 has been amended to recite the treatment of pollakiuria and/or urinary incontinence which is **not** responsive to COX-2 inhibition. Applicants note that the present specification teaches that the treatment of pollakiuria and/or urinary incontinence can be performed with compounds which are COX-2 inhibitors and with large conductance calcium-activated K channel openers at page 3, lines 3-8 of the specification.

Applicants respectfully submit that the amendment to claim 1 to recite the treatment of pollakiuria and/or urinary incontinence which is **not** responsive to COX-2 inhibition is not new matter for the following reasons. It is clear that the present specification **positively** recites that the present compounds can have both COX-2 inhibitory action and large conductance calcium-activated K channel opening action on page 3, lines 3-8 of the specification. Based on this amendment to claim 1, Applicants have excluded an embodiment

of the claimed method that was originally positively recited as being part of the invention. According to MPEP 2173.05(i), such a shift in the description of the invention is permissible. The relevant passage is as follows:

> Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) ("[the] specification, having described the whole, necessarily described the part remaining."). See also *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), *aff'd mem.*, 738 F.2d 453 (Fed. Cir. 1984).

New claim 6 recites the use of celecoxib which finds support in original claim 3.

New claims 7-11 are essentially identical to claims 1-5, except the last three lines of claim 7 recites:

> "wherein said pollakiuria and urinary incontinence is treatable by opening said large conductance calcium-activated K channel."

In this Reply, Applicants take the position that there are subsets of subjects having pollakiuria and urinary incontinence: a) one subset of subjects have pollakiuria and/or urinary incontinence which is/are treatable with a COX-2 inhibitor; b) one subset of subjects have pollakiuria and/or urinary incontinence which is/are treatable with a large conductance calcium-activated K channel opener; and c) one subset of subjects have pollakiuria and/or

urinary incontinence which is/are treatable with both a COX-2 inhibitor and a large conductance calcium-activated K channel opener. The last three lines of claim 7 clarify that the inventive compounds are used to treat the subset of subjects having pollakiuria and/or urinary incontinence which is/are treatable solely with a large conductance calcium-activated K channel opener.

No new matter has been added by way of the above amendment.

INTERVIEW

Applicants note with appreciation that the Examiner conducted an Interview with Applicants' representative on November 4, 2004. The Examiner was very helpful in clarifying the outstanding issues. On the Interview Summary form, the Examiner states:

> *Discussed proposed amendments to overcome enablement, indefiniteness and prior art rejections. The Examiner pointed out that compounds B, D and E disclosed in the cited U.S. patent are encompassed by the instant compounds of formula (I) of claim 1. The showing in declaration regarding different mechanism is not persuasive since the diseases to be treated are the same and the compounds used are the same.*

As the Examiner will note from the above-amendment, the claims have been limited to the specific compounds and diseases discussed during the Interview.

Further details of the interview are provided below.

The following sections correspond to the sections in the outstanding Office Action.

Section 2

Applicants note with appreciation that the Examiner has expanded the prior art search to include both the subject matter of Group I and Group III as defined in the March 18, 2004 communication from the Examiner.

Accordingly, the Examiner has considered the claims to the extent wherein the compounds of Formula I have ring A as benzene or a cycloalkane ring and ring Q as a monocyclic 5-membered ring containing either two nitrogen atoms as heteroatoms or nitrogen and oxygen as heteroatoms.

Section 4

The Examiner states that priority to Applicants' September 19, 2002 filing of the Provisional Application 60/411,749 has not been granted, since Applicants filed the non-provisional application on September 22, 2003 which is more than a year after the filing date of the Provisional Application.

The Examiner is advised that on Friday, September 19, 2003, the U.S. Patent and Trademark Office had an unexpected closure due to a hurricane, and as such, the USPTO was considered to be closed due to a Federal Holiday as set forth in the attached copy of the

Official Gazette (1275 Off. Gaz. Pat. & Trademark Off. 142 (Oct. 21, 2003)). Accordingly, Applicants' filing on the following Monday, September 22, 2003, was proper and is effectively within one year of the provisional filing date of September 19, 2002.

The Examiner is respectfully requested to acknowledge Applicants' claim for priority back to September 19, 2002 in the next communication.

Sections 5-8

Claims 1-5 are rejected under 35 U.S.C. 112, first and second paragraphs. Applicants respectfully traverse the rejection.

The Examiner indicated that Applicants' proposed amendment presented to the Examiner during the November 4, 2004 Interview would remove these rejections. In view of the fact that Applicants have limited the claims to essentially the subject matter discussed during the Interview, formal withdrawal of the rejections is respectfully requested.

Section 9

Claims 1-5 are rejected under 35 U.S.C. 102(a) as being anticipated by Leonardi et al. (U.S. Patent 6,440,963). Applicants respectfully traverse the rejection.

Leonardi et al. teaches a method of treating urinary incontinence based on COX2 inhibitory activity, whereas the present invention is directed to a method of treatment of pollakiuria or urinary incontinence based on BK (big potassium) or maxi-K channels opening action. In pollakiuria and urinary incontinence, there are various causes such as neurergic (cerebral apoplexy, Alzheimer's diseases, spinal damage, intervertebral disk pressure, etc.), urethremphraxis, urocystitis, vesical calculus, etc.

As evidence that the inventive compounds treat different diseases than the compounds of Leonardi et al., Applicants enclose herewith an executed Declaration Under 37 CFR 1.132.

In the Declaration, there is described experimental data in which experiments have been done with regard to the following three compounds using an acetic acid-induced pollakiuria model:

- Valdecoxib (selective COX2 inhibitor, having BK opening action; this invention)
- NS-398 (selective COX2 inhibitor, having no BK opening action)
- Indomethacin (non-selective COX2 inhibitor, having no BK opening action)

As a result, in the artificially created pollakiuria of this model, NS-398, which is a selective COX2 inhibitor did not show any effect. This is shown in Figure 1 of the Declaration.

Also, iberiotoxin (a BK inhibitor) was used with valdecoxib in combination, and the action by valdecoxib disappeared. This is shown in Figure 2 of the Declaration. That is, in this model, it could be understood that absolutely no action was shown in COX2 inhibitory action, and only BK opening action or COX1 inhibitory action shows treatment effects.

On the other hand, in the rhythmic bladder contraction model shown in Experimental Example 2 shown on pages 15-18 of the present specification, treatment effects can be obtained by COX2 inhibitory action, so that, in the experimental model, a disease that can be treated by COX2 inhibitory action and a disease that can be treated by BK opening action can be differentiated from each other.

In order to clarify that the present invention treats a subset of pollakiuria or urinary incontinence that is distinct from Leonardi et al., Applicants have amended the claims to recite that the instant method is to a treatment of pollakiuria and/or urinary incontinence which is **not** responsive to COX-2 inhibition as is required by Leonardi et al.

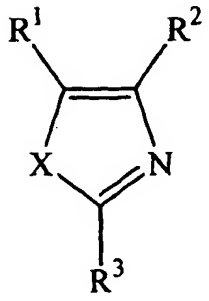
As the MPEP directs, all the claim limitations must be taught or suggested by the prior art to establish a *prima facie* case of anticipation. See MPEP §§ 2131. Since Leonardi et al. fail to teach

a method of treatment by BK opening action, nor the specific diseases treatable therefrom, a *prima facie* case of anticipation cannot be said to exist and withdrawal of the rejection is respectfully suggested.

Section 10

Claims 1-5 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Hongu (WO 02/083111). Applicants respectfully traverse the rejection.

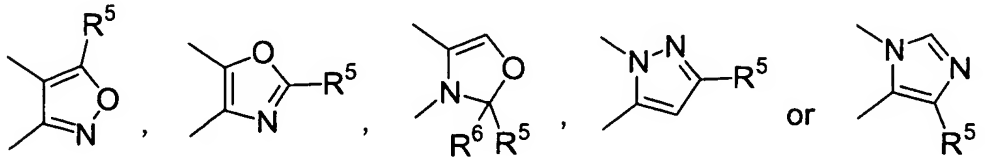
Hongu teaches the following genus of compounds (see abstract):



(I)

(57) Abstract: A large conductance calcium-activated K channel opener comprising as an active ingredient a nitrogen-containing 5-membered heterocyclic compound represented by the following formula (I): wherein X represents N-R^4, O or S, R^1 and R^2 each independently represent hydrogen, halogen, carboxyl, amino, lower alkyl, lower alkoxycarbonyl, lower alkenyl, cyclo-lower alkyl, carbamoyl, aryl, heterocyclic or heterocyclic-substituted carbonyl group, R^3 represents aryl, heterocyclic or lower alkyl group, and R^4 represents hydrogen or lower alkyl group.

The compounds defined in the newly amended claims have the following structures:



It appears that the 2nd ring that is an oxazole ring substituted at the 4- and 5-positions is encompassed by the genus of Hongu. However, Applicants note that the compounds of Hongu have rings at the 2- and 5-positions, whereas the inventive compounds require rings at the 4- and 5-positions.

In describing the requirements for rejection of a claim by anticipation, the Manual of Patent Examining Procedure (Section 2131) states:

> "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference (ref. omitted). The identical invention must be shown in as complete detail as is contained in the... claim (ref. omitted)."

The Examiner noted during the Interview, that Hongu fails to teach oxazole compounds having rings at the 4- and 5-positions. Accordingly, Hongu does not anticipate the claims, and as such, Applicants respectfully request that the rejection be withdrawn.

Furthermore, Hongu does not make obvious the inventive compounds, since the skilled artisan would find that the exemplified compounds of Hongu are a teaching away from the inventive group of compounds. In **all** of the exemplified compounds, Hongu has rings at the 2- and 5-positions, whereas the inventive compounds require rings at the 4- and 5-positions.

A reference which leads one of ordinary skill in the art away from the claimed invention cannot render it unpatentably obvious. *Dow Chem. Co. v. American Cyanamid Co.* 816 F2d 617, (CAFC 1987). In determining the scope and content of the prior art, and determining whether the prior art suggested the claimed invention, the references "must be read as a whole and consideration must be given where the references diverge and teach away from the claimed invention." *Akzo N.V. v. United States Int'l Trade Comm'n*, 1 USPQ2d 1241, 1246 (Fed. Cir. 1986); *In re Fine*, 5 USPQ2d 1596, 1598-99 (Fed. Cir. 1988).

Applicants respectfully submit that since the inventive oxazole compounds are not fairly taught by Hongu, the inventive method is patentable over Hongu.

Conclusion

In view of the above-amendments and comments, Applicants respectfully submit that the claims are in condition for allowance. A Notice to such effect is earnestly solicited.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicants respectfully petition for a three (3) months extension of time for filing a reply in connection with the present application, and the required fee of $980.00 is attached hereto.

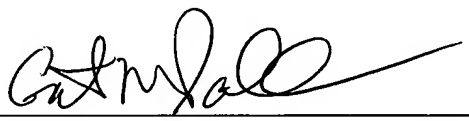
Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully

requested to contact **Garth M. Dahlen, Ph.D., Esq.** (Reg. No. 43,575) at the telephone number of the undersigned below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By 

Gerald M. Murphy, Jr., #28,977

Garth M. Dahlen, #43,575

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

GMM/GMD/mua
0283-0177P

Attachment: 1) 1275 Off. Gaz. Pat. & Trademark Off. 142 (Oct. 21, 2003)
2) Executed Declaration Under 37 CFR 1.132

United States Patent and Trademark Office OG Notices: 21 October 2003

Closing of the United States Patent and Trademark Office on Thursday, September 18, 2003, and Friday, September 19, 2003

In view of the official closing of the Federal Government offices in the Washington, D.C. metropolitan area, including the United States Patent and Trademark Office (USPTO), on Thursday, September 18, 2003, and Friday, September 19, 2003, the United States Patent and Trademark Office will consider Thursday, September 18, 2003, and Friday, September 19, 2003, a "Federal holiday within the District of Columbia" under 35 U.S.C. 21 and 37 C.F.R. 1.6, 1.7, 1.9, 2.2(d), 2.195, and 2.196. Any action or fee due on Thursday, September 18, 2003, or Friday, September 19, 2003, will be considered as timely for the purposes of, e.g., 35 U.S.C. 119, 120, 133 and 151, if the action is taken, or the fee is paid, on the next succeeding business day on which the USPTO was open, that is, Monday, September 22, 2003.

37 C.F.R. 1.6(a)(2) and 2.195(a)(4) provide that correspondenc deposited as Express Mail in accordance with 37 C.F.R. 1.10 or 2.198 will be considered as filed on the date of deposit with the United States Postal Service (USPS). Thus, any paper or fee properly deposited in accordance with 37 C.F.R. 1.10 or 2.198 with the Express Mail service of the USPS on Thursday, September 18, 2003, or Friday, September 19, 2003 (that is, as shown by a "date-in" of Thursday, September 18, 2003, or Friday, September 19, 2003, on the Express Mail mailing label) will be considered filed in the USPTO on its date of deposit in the Express Mail service of the USPS. 37 C.F.R. 2.195(a)(2) provides that trademark-related correspondence transmitted electronically to the USPTO will be considered filed in the USPTO on the date the USPTO receives the electronic transmission. Thus, trademark-related correspondence transmitted electronically on Thursday, September 18, 2003, and/or Friday, September 19, 2003, will be considered filed in the USPTO on the date the USPTO received the electronic transmission. Correspondence successfully received by the USPTO through the patent Electronic Filing System will receive the date as indicated on the Acknowledgment Receipt.

September 23, 2003

JAMES E. ROGAN
Under Secretary of Commerce for
Intellectual Property and
Director of the United States Patent and
Trademark Office